UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,076	09/07/2006	Bengt-Ake Bengtsson	05558.0036.PCUS00	2186

22930 7590 05/17/2010

HOWREY LLP - East
C/O IP DOCKETING DEPARTMENT
2941 FAIRVIEW PARK DR, SUITE 200
FALLS CHURCH, VA 22042-2924

EXAMINER	
BORGHEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
05/17/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,076	BENGTSSON, BENGT-AKE	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,8-15,18,25 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,8-15,18,25 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

The amendment after Final Rejection filed 14 April 2010 is acknowledged. The finality of the Office action mailed 28 December 2009 is hereby *withdrawn* in view of reference(s) U.S. Patent 7,304,029 and its WO document, WO 00/13650. Rejections based on the reference(s) follow.

Claim 1 is amended. Claims 28-30, 36, 37 and 39 are newly cancelled. Claims 1, 5, 6, 8-15, 18, 25 and 33 are under examination.

Claim Objections

Claim 1 is objected to because of the following informalities.

(i) For the sake of clarity, "hGH" should be inserted after "human growth hormone" in part (a) since the rest of the claims refer to hGH.

(ii) For continuity of lettering, the "(g)" should be amended to recite "(d)" in the last line of the claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 5, 6, 8, 10-15, 18 and 25 are rejected under 35 U.S.C. 102(b) and 102(e) as being anticipated by Scheepens et al., published as NEURONZ Ltd., WO 00/13650—on Applicants 1449 form dated 4 December 2007 and U.S. Patent No. 7,304,029, filed 27 February 2002—hereafter the '029 patent, as evidenced by Bauman (Endocrine Reviews, 1991; 12: 424-449—of record). The '029 patent teaches administration of GH or a variant of GH as a neuronal rescue agent for the treatment of neurological disorders, including multiple system atrophy at column 11, lines 51-67 and column 12, line 23 (p. 17, lines 3-35 of the '029 patent; p. 18, line 31 of WO 00/13650), thus meeting the limitation of claim 1. The GH may be "native [or] recombinantly produced," (see column 4, lines 30-35 of the '029 patent; p. 6, lines 32-36 through p. 7, lines 1-24 of WO 00/13650), thus meeting the limitations of claims 5 and 6. Since native GH is contemplated, it is inherent that it would comprise amino acids 177 to 191 of GH, thus meeting the limitation of claim 8.

Chemically synthesized GH is contemplated in the '029 patent at column 4, lines 33-56 and column 5, lines 39-44 (p. 6, lines 32-36 through p. 7, lines 1-24 of WO 00/13650), thus meeting the limitations of claim 14. Regarding claim 10, which recites a GH variant lacking the 15 amino acid residues from Glu32 to Glu46 of hGH; claim 13, which recites a dimer of hGH, and claims 14, 15 and 25, which recite chemically derivatized GH (e.g., deamidated GH), Bauman provides evidence that these forms are naturally occurring pituitary GH variants (see p. 428, Table 2; and p. 428, whole page through p. 430, left column; see also p. 432, whole page, under "oligomeric GH", which includes as discussion of naturally occurring non-covalent GH dimers). Regarding claims 11 and 12, which recite GH variants lacking the first 8 or 13 amino acid residues at the N-terminus, Bauman provides evidence that there is a GH variant lacking the first 43 amino acids (GH_{44-191}), which is possibly a native form of GH that has potent diabetogenic activity (see p. 430, right column, last paragraph through p. 431, left column, 1st paragraph). Since the '029 patent contemplates analogs and variants of GH (again, see column 4, lines 33-56 and columns 5 through 6 of the '029 patent and p. 6, lines 32-36 through p. 7, lines 1-24 of WO 00/13650), the analogs of GH recited in the instant claims, as evidenced by Bauman, are encompassed by the prior art. The reference by Bauman et al. shows that the characteristic analogs of GH, though not explicitly named by the Bauman reference, are disclosed inherently.

Regarding dose, the '029 patent teaches at column 5, lines 30-32 a dose range of 0.01 μg – 100 g of active ingredient (p. 13, line 17 of WO 00/13650), but more specifically, teaches a dose of 0.02 mg GH at column 9, lines 24 – 41 (p. 14, line 7 of

WO 00/13650). Note that 10 µl recombinant rat growth hormone containing 2 mg/ml. This is equivalent to:

?mg = 10 µl x 2mg/1000 µl 0.02 mg

This falls into the range recited in claim 18, (a) - (c), which are broadened by the term "about", thus 0.02 mg can be reasonably interpreted as being about 0.1 mg; 0.5 mg or 1 mg. Note that although the Example teaches rat growth hormone, treatment of humans is contemplated (see also column 4, lines 24-29 of the '029 patent; p. 6, lines 24-30 of WO 00/13650). Thus the claims do not teach anything over the prior art

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Scheepens et al. (the '029 patent and WO 00/13650) as applied to claims 1, 5, 6, 8, 10-15, 18 and 25 in the rejection above and further in view of Goeddel et al. (Nature, 1979; 281: 544-548—on Applicants 1449 form filed 7 November 2006). The first factor to consider when making a rejection under 35 U.S.C. 103(a) is to determine the scope and contents of the prior art. The teachings of the '029 patent and WO 00/13650 and how they meet the limitations of claims 1, 5, 6, 8, 10-15, 18 and 25 are discussed above. The teachings are applicable to the instant rejection, and are hereby incorporated. The second factor is to ascertain the differences between the prior art and the instant claims. The '029 patent and WO 00/13650 do not explicitly teach the methionyl GH. Goeddel et al. show how to make methionyl GH (see whole document; also Figure 1 at p. 545). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of the '029 patent and WO 00/13650 by making methionyl GH, as taught in Goeddel et al. because Goeddel et al. teach that "using a novel combination of chemically synthesized DNA and cDNA, a recombinant E. coli strain has been constructed which produces hGH in large amounts" (see p. 548, right column, last paragraph). The person of ordinary skill in the art would have been motivated to make methionyl hGH because Goeddel et al. teach that their recombinant hGH "compares favorably with the expression levels of other cloned genes using the same promoter in optimized conditions" and furthermore that it was produced in large amounts (see p. 548, right column, last 2 paragraphs of Goeddel). For this reason as well, the person of ordinary skill in the art could have reasonably expected success.

The teachings of Goeddel et al. indicate that the level of ordinary skill in the art of recombinant production of GH was high. Furthermore, the instant specification does not contain any objective evidence indicating that methionyl hGH has any surprising qualities with respect to the treatment of MSA. Thus claim 9 does not contribute anything non-obvious over the prior art.

Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Scheepens et al. (the '029 patent and WO 00/13650) as applied to claims 1, 5, 6, 8, 10-15, 18 and 25 in the rejection above and further in view of Johansson et al. (Neuroendocrinology, 1995; 61: 57-66). The first factor to consider when making a rejection under 35 U.S.C. 103(a) is to determine the scope and contents of the prior art. The teachings of the '029 patent and WO 00/13650 and how they meet the limitations of claims 1, 5, 6, 8, 10-15, 18 and 25 are discussed above. The teachings are applicable to the instant rejection, and are hereby incorporated. The second factor is to ascertain the differences between the prior art and the instant claims. The '029 patent and WO 00/13650 do not explicitly teach subcutaneous administration as recited in claim 33. Johansson et al. teach that GH treatment of GH deficient adults was known in the art to result in improved psychological well being, memory, concentration, etc. (see abstract and Introduction; pages 57-58). Based upon this knowledge the authors hypothesized that peripherally administered GH crossed the blood brain barrier. Patients were administered recombinant human GH 0.25 U/kg/week subcutaneously for four weeks (p. 58, right column, under "Treatment"), which resulted in a tenfold (significant;

p=0.002) increase of GH levels in the cerebrospinal fluid (CSF—see for instance, Table 2 at p. 62) and further, the authors ruled out this finding being a result of damage to the blood brain barrier or BBB (see p. 64, right column, bottom of 1st paragraph). The authors conclude that the ability of peripherally administered GH to improve psychological well being was likely a result of the ability of peripherally administered GH to cross the BBB (see p. 65, last paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of the '029 patent and WO 00/13650 by administering GH subcutaneously as taught by Johansson et al. because subcutaneous administration is far less invasive than intracerebroventricular (as taught in the '029 patent and WO 00/13650). The person of ordinary skill in the art would have been motivated to administer GH subcutaneously because it is a less invasive procedure and patients could be taught to self-administer, thus cutting down on the high cost associated with GH treatment. Further one of ordinary skill in the art would surmise that the less invasive procedure would lead to greater patient cooperation. For this reason as well, the person of ordinary skill in the art could have reasonably expected success. In summary, the teachings of Johansson et al. indicate that one of ordinary skill in the art was aware that subcutaneous GH treatment resulted in improved mental health measures and that GH was capable of crossing the blood brain barrier. Further, there is no evidence in the application as filed indicating any surprising or non-obvious results related to subcutaneous administration beyond what was known in the art. Thus claim 33 does not contribute anything non-obvious over the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

/Bridget E Bunner/
Primary Examiner, Art Unit 1647